Applicant : Jorg J. Goronzy et al.
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Attorney's Docket No.: 07039-170002

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-47. (Cancelled)

48. (Currently amended) A method for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said method comprising:

a) comparing the frequency of $CD4^+/CD28^{null}$ cells in said patient to a reference frequency to obtain information about said rheumatoid arthritis condition, and

b) determining if said patient is predisposed to develop severe disease based on said information and the presence or absence of ~~a polymorphism in~~ an HLA-DRB1 allele in said patient, wherein said HLA-DRB1 allele is an HLA-DRB1 *0401 allele, an HLA-DRB1 *0404 allele, an HLA-DRB1 *0405 allele, or an HLA-DRB1 *0408 allele.

49. (Previously presented) The method of claim 48, wherein said frequency of $CD4^+/CD28^{null}$ cells comprises the percent of $CD4^+$ cells that are CD28 negative.

50. (Previously presented) The method of claim 48, wherein said reference frequency is derived from the $CD4^+/CD28^{null}$ cell frequency from a population.

51. (Previously presented) The method of claim 50, wherein said population comprises a population of patients having a diffuse rheumatoid arthritis condition.

52. (Previously presented) The method of claim 50, wherein said population comprises a population of patients having a follicular rheumatoid arthritis condition.

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53. (Previously presented) The method of claim 50, wherein said population comprises a population of patients having a granulomatous rheumatoid arthritis condition.

54. (Previously presented) The method of claim 50, wherein said population comprises a population of healthy individuals.

55. (Previously presented) The method of claim 50, wherein said population comprises a population of patients having subcutaneous nodules.

56. (Previously presented) The method of claim 50, wherein said population comprises a population of patients having extra-articular involvement.

57. (Previously presented) The method of claim 50, wherein said population comprises a population of patients having major joint destruction.

58-59. (Cancelled)

60. (Currently amended) A method for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said method comprising:

a) determining the frequency of $CD4^+/CD28^{null}$ cells in said patient,

b) determining the presence or absence of ~~a polymorphism in~~ an HLA-DRB1 allele in said patient, <u>wherein said HLA-DRB1 allele is an HLA-DRB1 *0401 allele, an HLA-DRB1 *0404 allele, an HLA-DRB1 *0405 allele, or an HLA-DRB1 *0408 allele,</u>

c) comparing said frequency of $CD4^+/CD28^{null}$ cells to a reference frequency to obtain information about said rheumatoid arthritis condition, and

d) determining if said patient is predisposed to develop severe disease based on said information and said presence or absence of said <u>HLA-DRB1 allele</u> ~~polymorphism~~.

61.   (Currently amended) A kit for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said kit comprising:

a) a first binding pair member, wherein said first binding pair member has specific binding affinity for a $CD4^+/CD28^{null}$ cell marker such that the frequency of $CD4^+/CD28^{null}$ cells in said patient is determinable, and

b) an oligonucleotide primer, wherein said oligonucleotide primer has specific binding affinity for at least a portion of the locus containing an HLA-DRB1 allele such that the presence or absence of an HLA-DRB1 *0401 allele, an HLA-DRB1 *0404 allele, an HLA-DRB1 *0405 allele, or an HLA-DRB1 *0408 allele a polymorphism of said HLA-DRB1 allele in said patient is determinable.

62.   (Currently amended) The kit of claim 61, wherein said kit comprises a reference chart, wherein said reference chart contains information about $CD4^+/CD28^{null}$ cell frequencies such that said predisposition is determinable based on said frequency of $CD4^+/CD28^{null}$ cells in said patient and said presence or absence of said HLA-DRB1 *0401 allele, said HLA-DRB1 *0404 allele, said HLA-DRB1 *0405 allele, or said HLA-DRB1 *0408 allele polymorphism of said HLA-DRB1 allele.